L7 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2002 ACS

AB A review with 135 refs. The development and clin. use of the serotonin 5-HT1 receptor agonists, collectively known as the "triptans", has ushered in a new age for clinicians treating patients with migraine, as well as a new era for those who respond to the medicines. The triptans that are currently in use (sumatriptan, naratriptan, rizatriptan and zolmitriptan) and those in development [almotriptan, eletriptan and frovatriptan (SB-209509, VML-251)] all share a common pharmacol. of 5-HT1B/1D receptor agonist activity. Administration of a triptan during an acute migraine is aimed, via an interruption of the pathophysiol. of this disorder, at rapid and well tolerated relief of headache and assocd. symptoms of migraine. Migraine probably involves a combination of cranial vasodilatation, with peripheral trigeminal nerve activation and consequent excitation of trigeminal neurons within the caudal brainstem and upper cervical spinal cord (the trigeminocervical complex). Triptans may act by constricting cranial vessels through 5-HT1B receptors, by inhibiting peripheral trigeminal nerve afferents that innervate the vessels and **pain** -producing dura mater through 5-HT1D receptors, or by inhibiting central trigeminal neuronal traffic through 5-HT1D receptors, or by a combination of these mechanisms. Peripheral neuronal inhibition is likely to involve inhibition of calcitonin gene-related peptide (CGRP) release and perhaps to some degree inhibition of a trigeminally driven inflammatory process. Some aspects of the pharmacokinetics of the various triptans, such as the relationship between time to reach peak plasma concns. and half-lives and clin. efficacy, may reveal information about the fundamental processes at work in acute migraine. The triptans have been a source of considerable interest because they have provided important clues to the basic pathophysiol. of migraine and point to an important role for the CNS in this disorder.

AN 1998:749148 CAPLUS

DN 130:162588

TI Serotonin 5-HT1B/1D receptor agonists in migraine: comparative pharmacology and its therapeutic implications

AU Goadsby, Peter J.

CS Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK

SO CNS Drugs (1998), 10(4), 271-286
CODEN: CNDREF; ISSN: 1172-7047

PB Adis International Ltd.

DT Journal; General Review

LA English

RE.CNT 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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AB A review with 232 refs. Serotonin (5-hydroxytryptamine) is an important biogenic amine that fulfills the role of neurotransmitter and neuromodulator. It has been a focus of interest during the last decade. Its diversity of pharmacol. actions is related to a wide variety of receptors and effector mechanisms. Seven serotonin receptor families have been identified thus far. They are genetically different transmembrane proteins composed of several hundred amino acids. The majority of these are G-protein-coupled, except the 5-HT3 receptors, which are directly ligand gated to fast ion channels. Serotonin is widely distributed in the body within the central and peripheral nervous systems, smooth muscles, and platelets, in particular. Consequently, its effects manifest mainly in these organs and influence a wide variety of neural, vascular, smooth muscle, and platelet functions. (Melatonin, a physiol. active metabolite

of serotonin, is also instrumental in affecting many neural and hormonal functions.). Several selective agonists and particularly many selective antagonists have been developed for serotonin, which helped the serotonin receptor subtype classification. Some of these drugs are also used therapeutically in the treatment of migraine (eg, sumatriptan, which is a 5-HT1 receptor agonist), vascular disorders (5-HT2 antagonists), and nausea and vomiting (5-HT3 antagonists, eg, dolasetron, granisetron, ondansetron, and tropisetron), and have been investigated in gastrointestinal motility disorders (5-HT4 antagonists) and behavioral psychopathologies (5-HT1 agonists and 5-HT2-4 antagonists). Serotonin reuptake inhibitors are of particular clin. importance in the treatment of psychol. illnesses. Future use of these drugs is also envisioned in the treatment of certain types of **pain** syndromes. Awareness of the serotonergic drugs and the recognition of possible drug interactions among drugs that influence serotonergic mechanisms in humans are becoming increasingly important in the practice of anesthesiol.

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L7 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB A review with 108 refs. Antagonists of the serotonin 5-HT3 receptor are clin. effective antinausea and anti-emetic drugs for the treatment of cancer patients undergoing chemotherapy and for patients undergoing procedures involving general anesthesia. These compds. have also been evaluated for the treatment of irritable bowel syndrome, other **pain**-related disorders (including migraine) and a variety of central nervous system disorders (including anxiety, psychosis and the treatment of drug abuse). The status of research into potential clin. applications of these drugs is evaluated in this review. The evidence from preclin. and clin. studies is compared and avenues for future drug development using these compds. are discussed.
AN 1996:306379 CAPLUS
DN 125:89
TI 5-HT3 receptor antagonists
AU Silverstone, P. H.; Greenshaw, A. J.
CS Clinical Psychopharmacology Res. Unit, Univ. Alberta, Alberta, T6G 2B7, Can.
SO Expert Opin. Ther. Pat. (1996), 6(5), 471-481
CODEN: EOTPEG; ISSN: 1354-3776
DT Journal; General Review
LA English

L7 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB A review with 112 refs. There are conflicting results on the function of 5-HT in anxiety and depression. To reconcile this evidence, Deakin and Graeff have suggested that the ascending 5-HT pathway that originates in the dorsal raphe nucleus (DNR) and innervates the amygdala and frontal cortex facilitates conditioned fear, while the DRN-periventricular pathway innervating the periventricular and periaqueductal gray matter inhibits inborn fight/flight reactions to impending danger, **pain**, or asphyxia. To study the role of the DRN 5-HT system in anxiety, the authors microinjected 8-OH-DPAT into the DRN to inhibit 5-HT release. This treatment impaired inhibitory avoidance (conditioned fear) without affecting one-way escape (unconditioned fear) in the elevated T-maze, a new animal model of anxiety. The authors also applied 3 drug treatments that increase 5-HT release from DRN terminals: (1) intra-DRN microinjection of the benzodiazepine inverse agonist FG 4172, (2) intra-DRN microinjection of the excitatory amino acid kainic acid, and (3) i.p. injection of the 5-HT releaser and uptake blocker D-fenfluramine. All treatments enhanced inhibitory avoidance in the T-maze. D-Fenfluramine and intra-DRN kainate also decre

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AN 1997:365215 CAPLUS
DN 127:28509
TI Pharmacology of serotonin as related to anesthesia
AU Gyermek, Laszlo
CS Department of Anesthesiology, Harbor-UCLA Medical Center, UCLA School of Medicine, Torrance, CA, USA
SO J. Clin. Anesth. (1996), 8(5), 402-425
CODEN: JCLBE7; ISSN: 0952-8180
PB Elsevier
DT Journal; General Review
LA English

L7 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2002 ACS
AB A review and discussion, with 52 refs., of serotonin receptors in relation to migraine therapy which discusses: the peripheral pathways including trigeminal innervation of **pain**-sensitive intracranial structures, plasma protein extravasation and migraine

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AB A review with 135 refs. The development and clin. use of the serotonin 5-HT1 receptor agonists, collectively known as the "triptans", has ushered in a new age for clinicians treating patients with migraine, as well as a new era for those who respond to the medicines. The triptans that are currently in use (sumatriptan, naratriptan, rizatriptan and zolmitriptan) and those in development [almotriptan, eletriptan and frovatriptan (SB-209509, VML-251)] all share a common pharmacol. of 5-HT1B/1D receptor agonist activity. Administration of a triptan during an acute migraine is aimed, via an interruption of the pathophysiol. of this disorder, at rapid and well tolerated relief of headache and assocd. symptoms of migraine. Migraine probably involves a combination of cranial vasodilatation, with peripheral trigeminal nerve activation and consequent excitation of trigeminal neurons within the caudal brainstem and upper cervical spinal cord (the trigeminocervical complex). Triptans may act by constricting cranial vessels through 5-HT1B receptors, by inhibiting peripheral trigeminal nerve afferents that innervate the vessels and **pain** -producing dura mater through 5-HT1D receptors, or by inhibiting central trigeminal neuronal traffic through 5-HT1D receptors, or by a combination of these mechanisms. Peripheral neuronal inhibition is likely to involve inhibition of calcitonin gene-related peptide (CGRP) release and perhaps to some degree inhibition of a trigeminally driven inflammatory process. Some aspects of the pharmacokinetics of the various triptans, such as the relationship between time to reach peak plasma concns. and half-lives and clin. efficacy, may reveal information about the fundamental processes at work in acute migraine. The triptans have been a source of considerable interest because they have provided important clues to the basic pathophysiol. of migraine and point to an important role for the CNS in this disorder.
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